Complete Summary

GUIDELINE TITLE

Genetic evaluation and counseling of couples with recurrent miscarriage: recommendations of the National Society of Genetic Counselors.

BIBLIOGRAPHIC SOURCE(S)

Laurino MY, Bennett RL, Saraiya DS, Baumeister L, Doyle DL, Leppig K, Pettersen B, Resta R, Shields L, Uhrich S, Varga EA, Raskind WH. Genetic evaluation and counseling of couples with recurrent miscarriage: recommendations of the National Society of Genetic Counselors. J Genet Counsel 2005 Jun;14(3):165-81. [112 references] PubMed

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Recurrent miscarriage

GUIDELINE CATEGORY

Counseling
Evaluation
Screening

CLINICAL SPECIALTY

Family Practice
Internal Medicine
Medical Genetics
Obstetrics and Gynecology

INTENDED USERS

Advanced Practice Nurses
Allied Health Personnel
Physician Assistants
Physicians
Psychologists/Non-physician Behavioral Health Clinicians
Social Workers

GUIDELINE OBJECTIVE(S)

To provide recommendations for genetic evaluation and counseling of couples with recurrent miscarriage

TARGET POPULATION

Couples with recurrent miscarriage

INTERVENTIONS AND PRACTICES CONSIDERED

1. Personal medical and pregnancy history
2. Pathological evaluation of the fetal tissue and placenta (when possible)
3. Family medical history with appropriate documentation
4. Referrals to genetic specialist
5. Referrals to other specialists (e.g., maternal fetal medicine, reproductive endocrinology, gynecology)
6. Routine karyotyping of each partner
7. Testing female partner for:
    - Factor V Leiden and prothrombin G20210A mutations
    - Thrombophilias (anticoagulants protein C, protein S and antithrombin III, in women with a personal and/or family history of venous thromboembolism)
    - Alpha thalassemia (for individuals of Southeast Asian and Mediterranean ancestry with or without a personal or family history of fetal hydrops)
8. Assessment and addressing of psychosocial and cultural issues

MAJOR OUTCOMES CONSIDERED

- Miscarriage rate
- Successful pregnancy rate

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases
Searches of Unpublished Data

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The MEDLINE and PUBMED databases were searched for relevant English-language medical articles published from January 1983 to October 2004 using the key words: multiple miscarriages, chronic pregnancy loss, recurrent pregnancy loss, habitual aborter, fetal wastage, embryonic demise, and intrauterine fetal wastage. Input was sought from a patient advocacy group (RESOLVE) for multiple miscarriages.

Over 500 articles and their bibliographies were reviewed with emphasis on causes of miscarriages (i.e., infectious, teratogenic, thrombophilic, immunologic, cytogenetic, and single gene causes), and psychological and cultural issues related to pregnancy loss. Professional and patient resources were also reviewed.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

The literature was reviewed and evaluated for quality according to the categories outlined by the U.S. Preventive Services Task Force (1995):

I. Evidence obtained from at least one properly designed randomized controlled trial

II-1. Evidence obtained from well-designed controlled trials without randomization

II-2. Evidence obtained from well-designed cohort or case-control-analytic studies, preferably from more than one center or research group

II-3. Evidence obtained from multiple time series with or without the intervention

III. Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The authoring subcommittee consisted of experts in genetic counseling, medical genetics, maternal fetal medicine, internal medicine, family practice, infectious disease, cytogenetics, and coagulation disorders. Input was sought from a patient advocacy group (RESOLVE) for multiple miscarriages.

To develop the recommendations, members of the Inherited Pregnancy Loss Working Group (IPLWG) met four times at the University of Washington, Seattle, WA, and corresponded by telephone and e-mail. To obtain comments and suggestions about the proposed recommendations, a poster was presented at the American College of Medical Genetics (ACMG) annual meeting in March 2004, and oral presentations were given at the University of Washington Medical Genetics Grand Rounds and the National Society of Genetic Counselors (NSGC) annual education conference in October 2004.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

After review by the National Society of Genetic Counselors (NSGC) Genetics Services Committee, the full document was made available for review by the 2,072 members of the NSGC in December 2004. The NSGC full and associate membership includes genetic counselors, physicians, nurses, attorneys, PhD genetics professionals, and social workers. The NSGC Ethics Subcommittee (consisting of seven genetic counselors with training and/or experience in bioethics) and an attorney for the NSGC reviewed the revised document. No conflicts with the NSGC Code of Ethics were identified in the final document. The NSGC Board of Directors approved the final document in January 2005.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Recommendations for the Evaluation of Couples With Recurrent Miscarriage

The suggested evaluation and testing of couples with recurrent miscarriage is shown in Figure 1 of the original guideline document. It is important to ascertain the client's primary questions and concerns in order to mutually develop a plan to address these concerns.

I. Obtain the Personal Medical and Pregnancy History of the Consultand(s)
   - A. A sample medical and family history intake form is provided in Figure 2 of the original guideline document.
   - B. Thorough pathological evaluation of the fetal tissue and placenta should be pursued when possible according to the recommendations of the College of American Pathologists ("The examination of the placenta," 1991).

II. Document Family Medical History
   - A. Using standardized pedigree symbols, obtain first and second degree family history information from the consultand(s) (Bennett, 1999; Bennett et al., 1995). The standardized symbol for a spontaneous pregnancy loss is delta.
   - B. Targeted questions for the family medical history are included in the table below titled "Patient Interview Questions to Help Identify a Family History of Recurrent Miscarriage due to a Genetic Etiology".
   - C. Special attention should be made to first and second degree relatives who may have the history of mental retardation, learning disabilities, progressive muscle weakness, early cataracts, infertility, stillbirth, recurrent miscarriage, and coagulation disorders.
   - D. Record the ethnicity of both sets of grandparents.
   - E. Note any consanguinity; document on the pedigree the exact relationship of unions between relatives.
   - F. Verify reported family history of a genetic diagnosis with medical records, if possible.
   - G. Document results of thrombophilia panels, chromosomal studies, and molecular genetic testing.
   - H. Maintain family history confidentiality with respect to the consultand(s) and extended family members.

III. Referrals to other specialists (e.g., maternal fetal medicine, reproductive endocrinology, gynecology) should be considered to exclude maternal causes of recurrent miscarriage.

Patient Interview Questions to Help Identify a Family History of Recurrent Miscarriage due to a Genetic Etiology

Do any of your close biological relatives have a history of:

- Recurrent miscarriage (note gestation and fetal sex if known)?
- Stillbirth/neonatal death (obtain autopsy, as appropriate)?
- Babies born with abnormalities present at birth, failure to thrive, dysmorphic features, needing immediate surgery, decline of health?
- Difficulty in conceiving (infertility)?
- Uterine anomalies (e.g., fibroids, structural defects)?
- Mental retardation or developmental delay?
- Clotting disorder (e.g., thrombophilia)?
- Inherited disorders (e.g., incontinentia pigmenti, Rett syndrome, chondrodysplasia punctata, Aicardi syndrome, focal dermal hypoplasia of Goltz)?
- Diagnosis of alpha thalassemia (particularly for patients of Southeast Asian and Mediterranean ancestry)?

Are you and your partner blood relatives?

Genetic Evaluation and Testing Recommendations

Couples may have had a prior evaluation with a reproductive endocrinologist, gynecologist, maternal fetal medicine specialist, or other specialists, and testing (e.g., antiphospholipid antibodies, ultrasounds) may have been pursued previously to rule out other causes of recurrent miscarriage. A referral to a genetics specialist is warranted when the prior evaluations yielded normal results, and when the pregnancy, medical, and family history evaluations suggest the possibility of a genetic cause for the couple's recurrent miscarriage (RM), as well as to address any implications for other family members when a genetic etiology is identified. When possible, chromosomal analysis on fetal tissue from products of conception (POC) should be pursued immediately, in addition to a thorough pathological evaluation of the fetus and placenta. Routine karyotyping of each partner is standard and testing the woman for the factor V Leiden and prothrombin G20210A mutations should be considered. Testing for the less common thrombophilias (anticoagulants protein C, protein S, and antithrombin III) should be reserved for women with a personal and/or family history of venous thromboembolism. Testing for methylenetetrahydrofolate reductase (MTHFR) mutations in a woman with recurrent pregnancy loss is not justified, according to currently available studies. Genetic testing for alpha thalassemia is recommended for individuals of Southeast Asian and Mediterranean ancestry with or without a personal or family history of fetal hydrops. The use of specialized chromosomal studies such as comparative genome hybridization, subtelomeric studies, interphase studies on sperm and assays for skewed X-inactivation patterns are not warranted at this time, as their clinical utility has yet to be determined.

Psychosocial Issues

In addition to acknowledging and empathizing with the couple's pregnancy loss, it is also important to recognize the emotional pain that may be experienced by an older child who was anticipating the birth of his or her sibling. Children are affected by their parent's sadness, depression, grief, anger, guilt, sense of shame and stigmatization. Referrals to support groups, and marriage and family therapists should be made, as appropriate.

Psychosocial History of the Consultand(s)

Attempt to build a relationship with the proband and partner by validating, empathizing, and listening. Assess, record, and address the following in the probands and the partners:

A. Level of comprehension and communication
B. Level of education, employment, and social functioning, as appropriate
C. History of depression (e.g., disturbance in sleep pattern, anxiety, changes in appetite, weight gain or loss, fatigue, feelings of hopelessness, loss of libido, suicidal ideation)
D. History of alcohol or other drug use (especially a history of using alcohol or other drugs to self-medicate for depression and/or pain)
E. Grief reaction and perceived burden of having recurrent miscarriage
F. Coping skills
G. Family and community support systems

Cultural Issues

Genetic counselors and health care providers should explore and be respectful of beliefs regarding miscarriage, especially when working with patients from various cultures.

It is important to remember that the couple's personal beliefs regarding miscarriage may be different from their perceived cultural beliefs. Counseling and support revolves around the personal significance of the pregnancy loss to the woman and her partner.

Summary

Formulating a unified genetic evaluation and counseling recommendation for all couples with recurrent miscarriage is challenging. As there are several etiologies as well as psychosocial and cultural issues to consider, the assessment involves a team approach including various specialties (e.g., maternal fetal medicine, reproductive endocrinology, gynecology, genetics, psychology).

During the individual/couple's clinic visits, it is essential for the health care professional to obtain detailed pregnancy, medical, and family histories to determine the test that will most likely yield an informative result. Counseling of couples with RM must include acknowledging the profound emotional impact of pregnancy losses, as well as the implications for relatives when a genetic etiology is identified. Genetic counselors and other health professionals should have an awareness of the couple's personal and cultural beliefs regarding miscarriage. Acknowledging the couple's grief and providing realistic assessments of their chance of reproductive success are important even if the underlying cause of the RM is not identified. In addition, referrals to support groups and professional therapists should be made as appropriate.

CLINICAL ALGORITHM(S)

An algorithm titled "Suggested evaluation and testing of couples with recurrent miscarriage" is provided in the original guideline document.

EVIDENCE SUPPORTING THE RECOMMENDATIONS

REFERENCES SUPPORTING THE RECOMMENDATIONS

References open in a new window

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

All supporting evidence is class III, opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees. No supporting literature of categories I and II was identified.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate evaluation and counseling of couples with recurrent miscarriage to increase the outcome for a successful live birth

POTENTIAL HARMS

Not stated

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

The genetic counseling recommendations of the National Society of Genetic Counselors (NSGC) are developed by members of the NSGC to assist practitioners and patients in making decisions about appropriate management of genetic concerns. Each practice recommendation focuses on a clinical or practice issue and is based on a review and analysis of the professional literature. The information and recommendations reflect scientific and clinical knowledge current as of the submission date and are subject to change as advances in diagnostic techniques, treatments, and psychosocial understanding emerge. In addition, variations in practice, taking into account the needs of the individual patient and the resources and limitations unique to the institution or type of practice, may warrant approaches, treatments, or procedures alternative to the recommendations outlined in this document. Therefore, these recommendations should not be construed as dictating an exclusive course of management, nor does use of such recommendations guarantee a particular outcome. Genetic counseling recommendations are never intended to displace a health care provider's best medical judgment based on the clinical circumstances of a particular patient.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Chart Documentation/Checklists/Forms
Clinical Algorithm

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Laurino MY, Bennett RL, Saraiya DS, Baumeister L, Doyle DL, Leppig K, Pettersen B, Resta R, Shields L, Uhrich S, Varga EA, Raskind WH. Genetic evaluation and counseling of couples with recurrent miscarriage: recommendations of the National Society of Genetic Counselors. J Genet Counsel 2005 Jun;14(3):165-81. [112 references] PubMed

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2005 Jun

GUIDELINE DEVELOPER(S)

National Society of Genetic Counselors

SOURCE(S) OF FUNDING

This project was supported by the National Society of Genetic Counselors, Inc.

GUIDELINE COMMITTEE

Not stated

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the National Society of Genetic Counselors Web site.

Print copies: Available from the National Society of Genetic Counselors, 401 N. Michigan Avenue, Chicago, IL 60611; Web site: www.nsgc.org.

AVAILABILITY OF COMPANION DOCUMENTS

A sample recurrent miscarriage intake form is available in the original guideline document.

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on March 23, 2006. The information was verified by the guideline developer on May 3, 2006.

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